CLAIMS

We claim:

1. A heparin-binding peptide of the formula $R_1(X_1B_1B_2X_2B_3X_3Y_1R_2)_nR_3$ or $R_1(X_1B_1B_2B_3X_2X_3B_4X_4Y_1R_2)_nR_3$ wherein:

X_1, X_2, X_3, and X_4 are independently selected from the group consisting of hydropathic amino acids;

B_1, B_2, B_3, and B_4 are independently selected from the group consisting of basic amino acids;

Y_1 is independently

(i) zero amino acid residues, or

(ii) one to ten amino acid residues, wherein at least one of said amino acid residues is proline;

n is an integer from one to ten;

R_1, R_2, and R_3 are independently selected segments containing from zero to twenty amino acid residues, provided, at least one of the segments R_1, R_2, and R_3 comprises at least one hydrophobic amino acid residue; and

wherein said heparin-binding peptide optionally comprises an amino-terminal protecting group or a carboxy-terminal protecting group or both an amino-terminal protecting group and a carboxy-terminal protecting group.

2. The heparin-binding peptide of claim 1, wherein X_1, X_2, X_3, and X_4 are independently selected from the group consisting of alanine, asparagine, cysteine, glutamine, glycine, histidine, isoleucine, leucine, proline, serine, tyrosine, threonine, tryptophan, methionine, phenylalanine, and valine.

3. The heparin-binding peptide of claim 2, wherein at least one of X_1, X_2, X_3, and X_4 is alanine.

4. The heparin-binding peptide of claim 3, wherein X_1 is alanine.

5. The heparin-binding peptide of claim 3, wherein X_1, X_2, and X_3 are alanine.

6. The heparin-binding peptide of claim 1, wherein at least one of B_1, B_2, B_3, and B_4 is arginine.

7. The heparin-binding peptide of claim 6, wherein B_1 is arginine.

8. The heparin-binding peptide of claim 7, wherein B_2, B_3, and B_4 are lysine.

9. The heparin-binding peptide of claim 1, wherein at least one of B_1, B_2, B_3, and B_4 is lysine.

10. The heparin-binding peptide of claim 9, wherein B_1 is lysine.

11. The heparin-binding peptide of claim 10, wherein B_2 is lysine and B_3 is arginine.

12. The heparin-binding peptide of claim 1, wherein at least one of B_1, B_2, B_3, and B_4 is histidine.

13. The heparin-binding peptide of claim 1, wherein R_1, R_2, and R_3 are independently selected from the group consisting of amino acid sequences SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:43, and SEQ ID NO:44.

14. The heparin-binding peptide of claim 1, wherein said at least one hydrophobic amino acid is selected from the group consisting of valine, leucine, and isoleucine.

15. The heparin-binding peptide of claim 1, wherein said hydrophobic amino acid residue is at a terminus of said peptide.

16. The heparin-binding peptide of claim 1, wherein said peptide comprises at least about thirty amino acid residues.

17. The heparin-binding peptide of claim 1, wherein said peptide comprises less than about two-hundred fifty amino acid residues.

18. The heparin-binding peptide of claim 1, wherein said peptide binds with a dissociation constant of about 1000 nM or lower to at least one heparin selected from the group consisting of unfractionated heparin, low molecular weight heparin, non-heparin glycosaminoglycan, and heparin pentasaccharide.

19. The heparin-binding peptide of claim 18, wherein said peptide neutralizes heparin activity by at least about 10%.

20. The heparin-binding peptide of claim 19, wherein said peptide neutralizes heparin activity by at least about 30%.

21. The heparin-binding peptide of claim 20, wherein said peptide neutralizes heparin activity by at least about 50%.

22. The heparin-binding peptide of claim 18, wherein said peptide comprises at least one amino acid D-isomer.

23. The peptide of claim 18, wherein said peptide comprises a proline residue.

24. The heparin-binding peptide of claim 23, wherein said peptide is selected from the group consisting of amino acid sequences SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, and SEQ ID NO:21.

25. The heparin-binding peptide of claim 1, wherein said peptide is a synthetic peptide.

26. The heparin-binding peptide of claim 1, wherein said peptide is selected from the group consisting of amino acid sequences SEQ ID NO:1, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, and SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:45, SEQ ID NO:46, and SEQ ID NO:47.

27. The heparin-binding peptide of claim 1, wherein ($X_1B_1B_2X_2B_3X_3Y_1R_2$) has the amino acid sequence SEQ ID NO:41.

28. The heparin-binding peptide of claim 1, wherein ($X_1B_1B_2B_3X_2X_3B_4X_4Y_1R_2$) has the amino acid sequence SEQ ID NO:29.

29. The heparin-binding peptide of claim 1, wherein R_2 is selected from the group consisting of amino acid sequences CA and SEQ ID NO:26.

30. A pharmaceutical composition comprising at least one peptide of claim 1 and a pharmaceutically-acceptable carrier.

31. A method of reducing plasma heparin levels in a subject in need of such treatment, said method comprising administering to said subject a pharmaceutical composition comprising at least one heparin-binding peptide according to claim 1, in an amount effective to reduce said plasma heparin levels in said subject.

32. The method of claim 31, wherein said subject is a human.

33. A method of reducing the anticoagulant effects of a heparin in a subject, said method comprising administering to said subject a pharmaceutical composition comprising at least one heparin-binding peptide according to claim 1, in an amount effective to reduce the anticoagulant effects of said heparin.

34. The method of claim 33, wherein said subject is a human.

35. A heparin-binding peptide of the formula $C(X_1B_1B_2B_3X_2X_3B_4X_4)_nC$ wherein:

X_1, X_2, X_3, and X_4 are independently selected from the group consisting of hydropathic amino acids;

B_1, B_2, B_3, and B_4 are independently selected from the group consisting of basic amino acids;

C is cysteine;

n is an integer from one to ten;

said peptide is optionally cyclized via a disulfide bond formed between said cysteine residues; and

said peptide optionally comprises an amino-terminal protecting group or a carboxy-terminal protecting group or both an amino-terminal protecting group and a carboxy-terminal protecting group.

36. The heparin-binding peptide of claim 35, wherein the segment $X_1B_1B_2B_3X_2X_3B_4X_4$ has the amino acid sequence SEQ ID NO:29.

37. The heparin-binding peptide of claim 36, wherein n is 4.

38. The heparin-binding peptide of claim 35, wherein said peptide binds with a dissociation constant of about 1000 nM or lower to at least one heparin selected from the group consisting of unfractionated heparin, low molecular weight heparin, non-heparin glycosaminoglycan, and heparin pentasaccharide.

39. The heparin-binding peptide of claim 38, wherein said peptide neutralizes heparin activity by at least about 10%.

40. The heparin-binding peptide of claim 39, wherein said peptide neutralizes heparin activity by at least about 30%.

41. The heparin-binding peptide of claim 40, wherein said peptide neutralizes heparin activity by at least about 50%.

42. The heparin-binding peptide of claim 38, wherein said peptide comprises at least one amino acid D-isomer.

43. The heparin-binding peptide of claim 35, wherein said peptide has the amino acid sequence SEQ ID NO:34.

44. A pharmaceutical composition comprising at least one peptide of claim 35 and a pharmaceutically-acceptable carrier.

45. A method of reducing plasma heparin levels in a subject in need of such treatment, said method comprising administering to said subject a

pharmaceutical composition comprising at least one heparin-binding peptide according to claim 35, in an amount effective to reduce said plasma heparin levels in said subject.

46. The method of claim 45, wherein said subject is a human.

47. A method of reducing the anticoagulant effects of a heparin in a subject, said method comprising administering to said subject a pharmaceutical composition comprising at least one heparin-binding peptide according to claim 35, in an amount effective to reduce the anticoagulant effects of said heparin.

48. The method of claim 47, wherein said subject is a human.

49. A conjugate comprising a heparin-binding peptide according claim 1 or claim 35 conjugated to at least one active agent.

50. A conjugate according to claim 49, wherein said active agent is selected from the group consisting of a cytotoxic active agent, a hormone, a peptide, an antibiotic, a nucleic acid, a radionuclide, an anti-inflammatory active agent, and a polysaccharide.

51. A method of delivering at least one active agent to a tissue or cell displaying high levels of glycosaminoglycans or proteoglycans, said method comprising administering a pharmaceutical composition comprising at least one conjugate of claim 49 and a pharmaceutically acceptable carrier, wherein said conjugate binds to said glycosaminoglycans or proteoglycans and delivers said at least one active agent to said tissue or cell.

52. The method of claim 51, wherein said tissue or cell is selected from the group consisting of blood vessels, connective tissue, cartilage and endothelial cells.

53. A method of treating a mast cell serine protease-associated disorder in a subject, said method comprising administering to said subject a pharmaceutical composition comprising at least one heparin-binding peptide according to claim 1 or claim 35 and a pharmaceutically acceptable carrier in an amount effective to treat the mast cell serine protease-associated disorder.

54. The method of claim 53, wherein said protease is chymase or tryptase.

55. The method of claim 54, wherein said mast cell serine protease-associated disorder is selected from the group consisting of inflammation, allergic reaction, rheumatoid arthritis, and microbial infection.

56. A method of treating a microbial infection in a subject, said method comprising administering to said subject a pharmaceutical composition comprising at least one heparin-binding peptide according to claim 1 or claim 35 in an amount effective to treat the infection.

57. The method of claim 56, wherein said pharmaceutical composition is administered topically.

58. The method of claim 56, wherein the microbial infection is a bacterial infection or a fungal infection.

59. The method of claim 58, wherein the bacterial infection is selected from the group consisting of an *Enterococcus faecalis* infection, an *Escherichia coli infection*, a *Pseudomonas aeruginosa* infection, and a *Proteus mirabilis* infection.

60. The method of claim 58, wherein the fungal infection is a *Candida albicans* infection.

61. A conjugate comprising a heparin-binding peptide according to claim 1 or claim 35 conjugated to at least one carrier molecule.

62. A conjugate according to claim 61, wherein said carrier molecule is selected from the group consisting of collagen, hyaluronic acid and agarose.

63. A conjugate according to claim 61, wherein said carrier molecule is further conjugated to a surgical sheet or mat.

64. A method of reducing the anticoagulant effects of a heparin in a subject, said method comprising administering to said subject a pharmaceutical composition comprising at least one conjugate according to claim 61 and a pharmaceutically acceptable carrier, in an amount effective to reduce the anticoagulant effects of said heparin.

65. The method of claim 64, wherein said pharmaceutical composition is administered locally.